Columbia University
in the City of New York
[NEW YORK 27, N. Y.]
DEPARTMENT OF ZOÖLOGY

May 14

Dear Josh,

We were in Woods Hole a couple of weeks ago and saw no signs of houses for rent. If you havn't already done so you might get results by writing to Homer Smith, the lab. business manager (he's not the Homer Smith) or Miss Mary E. Broderick who may have rooms to rent, or Mrs. Tawell likewise. No special addresses are necessary as these people are well known to postal authorities.

If you have talked with Szilard recently you know that our experiments with the colicine hypothesis of adaptive leaps about which I was all excited simply won't repeat. Apparently we were dealing with some curious real phenomenon however, which I'd rather tell you about verbally, since its complex yet trivial. The basis for the adaptive leaps is faster growth rate, but we were never able to demonstrate the difference turbidometrically. It is easily shown by plating of less dense cultures. This raises the question of how the cultures still possess adaptive potential despite their long phylogenetic history. The answer (as you will have guessed) is that the adaptive value of the different types we have recovered is dependent on the medium. For example, if 3 overgrows 0 on synthetic medium, just the reverse is seen on nutrient broth. So unless the process can be continued by some form of interaction, PS will end when we have the last word in adaptation to a given medium and the mutation rates will have their way. We have tried to fool the bacteria by alternating the medium twice a day, but this doesn't seem to work.

As for theories of PS, we have no detailed one. Here is an attempt: Let X_1, X_2, X_3 etc. represent unselected mutants arising with rate, a, from parental populations N_1, N_2, N_3 etc. where the latter arise successively from each other once in every interval, i, and differer from each other by a constant growth rate increment, k. i may be expressed in generations, g. If we start with a single N_1 cell:

I think this is unlikely, too.

$$N_1+N_2+N_3+\dots+N_n+\dots = 2^g + 2^{k(g-i)} + 2^{k^2(g-2i)} + \dots + 2^{k^n[g-(n-1)i]} + \dots$$

and,

$$X_1+X_2+X_3+\dots+X_n+\dots = ga2^g + (g-i)a2^{k(g-i)} + (g-2i)a2^{k^2(g-2i)} + \dots + [g-(n-1)]a2^{k^n[g-(n-1)]} + \dots$$

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and

$$\frac{X_1 + X_2 + X_3 + \ldots + X_n + \ldots}{N_1 + N_2 + N_3 + \ldots + N_n + \ldots}$$

is the ratio we are looking at. This ratio will have an equilibrium hwen g is large because it will consist essentially of the ratio of the last few terms of each series (we are ignoring terms with negative exponents, i. e. those in which g-(n-1)i is zero or less, and we are sampling out the first few terms because they are so small compared to the next few, and the number of terms which can be ignored increases as g increases). This model is not a very realistic one however, since it does not correctly represent the origin of the successive types by mutation, but assumes each arises only once. I don't think it will be difficult to construct a suitable model based on this general approach. Here's a different way of looking at it: assume that a growth rate which is the mean of a distribution of growth rates of the bacteria is the apparent growth rate of a culture. This mean steadily increases due to mutation. Each time a mutant of higher adaptive value appears there will be a time lapse before indicator mutants, X, are produced from the new clone. Consequently the average growth rate of the indicator mutants, X, will always be less than that of the whole culture. In other words, the mean for indicator mutants will always lag behind the mean for the whole culture. (An indicator mutant is any kind that doesn't affect the growth rate). Note that none of these schemes leads to a mutational equilibrium, in fact I haven't even had to consider back-mutation of X. Of course, if the equilibrium predicted by the first scheme is so high that growth rate mutations occur frequently in X bacteria, the stability is lost.

We heard recently from F.J. that the lac phenomenon was due to selection as you had indicated. Everyone is well here, but I am overwhelmed by mundane academic duties. Regards to Esther. See youboth soon.

Kim

P.S. I will send you the radiation ms within a few days.

P.P.S. Lil suggests Mrs. Kenyon*, Mrs. Riley* and Mrs. J. McInnes in Woods Hole. *Initials unknown